## CLAIMS

1. Oligomeric conjugate positively charged, containing an oligomer with a polymerization degree (PD) from 5 to 50, preferably 10 to 40 and more preferably 20, formed from monomeric components having free $NH_3^+$ in a number equal to or higher than 50 % of the polymerization degree,

said oligomer being as follows :

- the free $NH_3^+$ of the above-mentioned components are substituted in a ratio of at least 50 %, advantageously from 60 % to 95 %, particularly 80 to 90 % (this ratio being determined by nuclear magnetic resonance), by protonable residues in a weak acid medium, leading in such a weak acid medium to a destabilization of cellular membranes,

- the above-mentioned protonable residues possess in addition the following properties :

→ they contain a functional group enabling them to be linked to the above-mentioned oligomer,

→ they do not correspond to a recognition signal recognized by a cellular membrane receptor,

→ they can comprise at least one free $NH_3^+$ group,

- the free $NH_3^+$ of the above-mentioned monomers can be also substituted by an uncharged residues leading to a reduction of the number of positive charges in comparison to the same oligomeric before substitution,

- molecules constituting a recognition signal recognized by a membrane cellular receptor may be present :

→ either by substitution of some of the free $NH_3^+$ of the above-mentioned monomers,

→ either on some of the uncharged residues leading to a reduction of the number of charges,

→ either on some of the above-mentioned protonable residues leading to a destabilization of the cellular membranes,

→ or by substitution of the free $NH_3^+$ (if it is present) of the above-mentioned protonable residues leading to a destabilization of the cellular membrane,

provided that :

1) the total number of the non substituted $NH_3^+$ functions is of at least 50 % of the polymerization degree,

2) the number of monomers initially carrying free $NH_3^+$ is substituted in a ratio of at least 50 % of the polymerization degree by residues leading to a destabilization of the cellular membrane.

2. Oligomeric conjugate according to claim 1, wherein the protonable residues leading to a destabilization of cellular membranes, present the additional properties :

- they are weak bases the pK of which in aqueous medium is lower than 8, so that a proportion higher than 50 % of these bases linked to a cationic oligomer is not protonated in a neutral medium of pH 7.4.

3. Oligomeric conjugate complex according to claim 1, wherein the protonable residues leading to a destabilization of cellular membranes, present the additional properties:

- they belong to the group of compounds comprising an imidazole ring,
- they belong to the group of quinolins,
- they belong to the group of pterins,
- they belong to the groupe of pyridins.

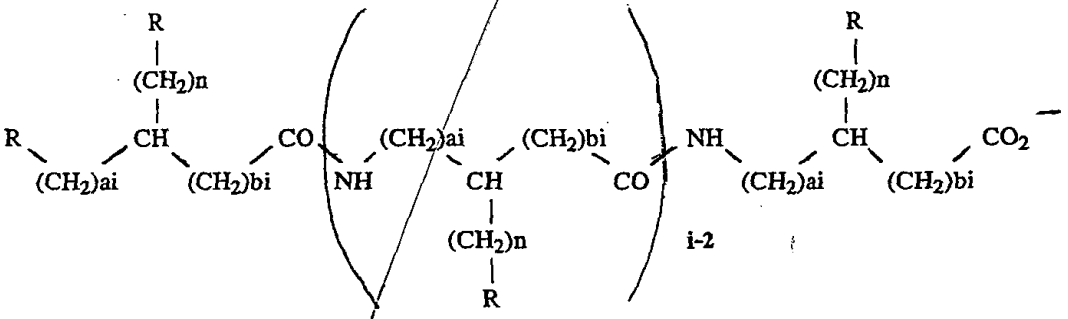
4. Oligomeric conjugate according to anyone of claims 1 to 3, wherein the protonable residues leading to a destabilization of the cellular membranes are :

- alkylimidazoles in which the alkyl radical comprises from 1 to 10, particularly from 2 to 6 carbon atoms, and in which only one of the nitrogen atoms of the imidazole ring is substituted.

5. Oligomeric conjugate according to anyone of claims 1 to 4, wherein the protonable residues leading to a destabilization of cellular membranes are chosen from :

histidine, 4-carboxymethyl-imidazole,
3-(1-methyl-imidazol-4yl)-alanine, 3-(3-methyl-imidazol-4yl)-alanine,
2-carboxy-imidazole, histamine, 3-imidazol-4yl)-L-lactic acid,
2-(1-methyl-imidazol-4yl)ethylamine, 2-(3-metyl-limidazol-4yl)ethylamine,
β-alanyl-histidine-(carnosine), 7-chloro-4(amino-1-methylbutylamino)-quinoline,
$N^4$-(7-chloro-4-quinolinyl)-1,4-pentanediamine,
8-(4-amino-1-methylbutylamino)-6-methoxy-quinoline (primaquine),
$N^4$-(6-methoxy-8-quinolinyl)1,4-pentanediamine, quininic acid,
quinoline carboxylic acid, pteroïc acid, nicotinic acid, quinolinic acid.

6. Oligomeric conjugate according to anyone of claims 1 to 5, wherein the oligomeric conjugate contains an oligomer of the following formula :




i-2

wherein * ai is an integer varying from 0 to 10,

* bi is an integer varying from 0 to 10,

* i = degree of polymerization from 5 to 50, and particularly 10 to 40, and preferably 20,

* n = is an integer varying from 1 to 6, and preferably 4,

* R represents in a ratio of 50 % to 100 % (corresponding to a number u)

→ NH-CO-$(CH_2)$n'-CH-R'
|
$(CH_2)$m
|
B

or

→ NH-CO-CH-$(CH_2)$n'-R'
|
$(CH_2)$m
|
B

or

→ NH-CO-$(CH_2)$n'-CH-$(CH_2)$n"-R'
|
$(CH_2)$m
|
B

m is an integer varying from 1 to 6,

n' is an integer varying from 0 to 6,

n" is an integer varying from 0 to 6,

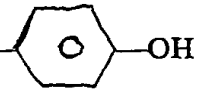
B is a weak base as defined according to anyone of claims 2 to 4,

R' represents $NH_3^+$ (corresponding to a number p),
or NH (corresponding to a number q) substituted by

-CO-$CH_3$

-CO-(CHOH)rH r being an integer from 1 to 15, and preferably 1 to 7

-CO-$(CH_2)$s-(CHOH)rH r being an integer from 1 to 15, and preferably 1 to 7, and s being an integer from 1 to 6, and preferably 6

-CO-$CH_2$-  -OH

-$SO_2$-Flu

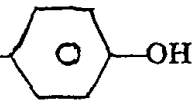
-CO-Flu

-CS-NH-Flu

Flu being a fluorescent molecule

* R represents in a ratio of 0 % to 50 % (corresponding to f ; $0 < f \leq u$)

- $NH_3^+$ (corresponding to a number j),
- NH (corresponding to a number k), substituted by

| | |
|---|---|
| $-CO-CH_3$ | |
| $-CO-(CHOH)rH$ | r being an integer from 1 to 15, and preferably 1 to 7 |
| $-CO-(CH_2)s-(CHOH)rH$ | r being an integer from 1 to 15,and preferably 1 to 7, and s being an integer from 1 to 6, and preferably 6 |
| $-CO-CH_2-$  $-OH$ | |
| $-SO_2$-Flu | |
| -CO-Flu | |
| -CS-NH-Flu | |

Flu being a fluorescent molecule

- H (corresponding to a number h)
- $(CH_2)$ nH, (corresponding to a number h) — n being an integer from 1 to 6
- $(CH_2)$ n-OH (corresponding to a number h) — n being an integer from 1 to 6
- $(CH_2)$ n-SA' A' = H, $CH_3$ or  (corresponding to a number h) — n being integer from 1 to 6

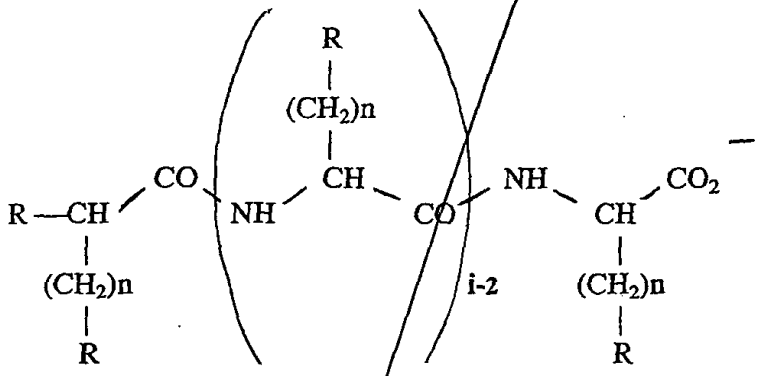
with
- $i = u + j + k + h$
- total number of $\alpha$ $NH_3^+ = p = u-q$
- total number of $\omega$ $NH_3^+ = j = f-(k + h)$
- total number of $NH_3^+ = m = p + j+1$

with the proviso that :

1) u≥ i/2

2) m ≥ i/2

7. Oligomeric conjugate according to anyone of claims 1 to 6, wherein the oligomeric conjugate contains an oligomer of the following formula :



wherein

* i = degree of polymerization from 5 to 50, and particularly 10 to 40, and preferably 20,

* n = is an integer varying from 1 to 6, and preferably 4,

* R represents in a ratio of 50 % to 100 % (corresponding to u)

→ NH-CO-(CH$_2$)n'-CH-R'
|
(CH$_2$)m
|
B or

→ NH-CO-CH-(CH$_2$)n"-R'
|
(CH$_2$)m
|
B or

→ NH-CO-$(CH_2)$n'-CH-$(CH_2)$n"-R'
|
$(CH_2)$m
|
B

m is an integer varying from 1 to 6,

n' is an integer varying from 0 to 6,

n" is an integer varying from 0 to 6,

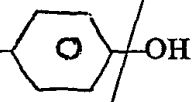
B is a weak base as defined according to anyone of claims 2 to 4,

R' represents $NH_3^+$ (corresponding to a number p),
or NH (corresponding to a number q) substituted by

-CO-$CH_3$

-CO-(CHOH)rH — r being an integer from 1 to 15, and preferably 1 to 7

-CO-$(CH_2)$s-(CHOH)rH — r being an integer from 1 to 15, and preferably 1 to 7, and s being an integer from 1 to 6, and preferably 6



-$SO_2$-Flu

-CO-Flu

-CS-NH-Flu

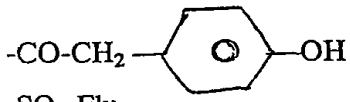
Flu being a fluorescent molecule

* R represents in a ratio of 0 % to 50 % (corresponding to f : $0 < f \leq 1$)
- $NH_3^+$ (corresponding to a number j),
- NH (corresponding to a number k), substituted by

-CO-$CH_3$

-CO-(CHOH)rH — r being an integer from 1 to 15, and preferably 1 to 7

-CO-$(CH_2)$s-(CHOH)rH r being an integer from 1 to 15, and preferably 1 to 7, and s being an integer from 1 to 6, and preferably 6



-$SO_2$-Flu

-CO-Flu

-CS-NH-Flu

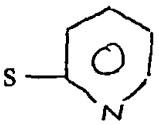
Flu being a fluorescent molecule

- H (corresponding to a number h)
- $(CH_2)_n$H, n being an integer from 1 to 6

(corresponding to a number h)

- $(CH_2)_n$-OH n being an integer from 1 to 6

(corresponding to a number h)

- $(CH_2)_n$-SA' A' = H, $CH_3$ or 

(corresponding to a number h) n being integer from 1 to 6

with
- i = u + j + k + h
- total number of α $NH_3^+$ = p = u-q
- total number of ω $NH_3^+$ = j = f-(k + h)
- total number of $NH_3^+$ = m = p + j + 1

with the proviso that :

1) u ≥ i/2

2) m ≥ i/2

8. Oligomeric conjugate according to anyone of claims 1 to 7, wherein the oligomeric conjugate contains an oligomer of the formula according to claim 7, wherein

i = 19 n = 4 (u) R= NH-CO-$(CH_2)$n' -CH-$(CH_2)$n"-R'

$(CH_2)$m

B

wherein

n' = n" = 0

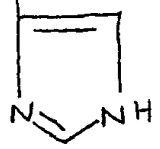
R' = $NH^+_3$

m = 1

B = imidazole

R = NH-CO-CH- $NH_3^+$

$CH_2$



(f) R = $NH^+_3$

u = 12

j = 7

or

i = 19 n = 4 (u) R= NH-CO-$(CH_2)$n' -CH-$(CH_2)$n"-R'

$(CH_2)$m

B

wherein

n' = n" = 0

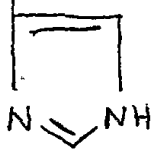
R' = $NH^+_3$

m = 1

B = imidazole

R = NH-CO-CH- $NH_3^+$

$CH_2$



(f) R = $NH^+_3$

u = 16

j = 3

or

i = 19 n = 4 (u) R= NH-CO-$(CH_2)n'$-CH-$(CH_2)n''$-R'

|
$(CH_2)m$
|
B

wherein

n' = n" = 0

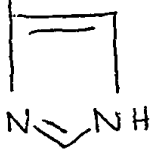
R' = $NH^+_3$

m = 1

B = imidazole

R = NH-CO-CH- $NH_3^+$

|
$CH_2$



(f) R = $NH^+_3$

u = 19

j = 0

or

i = 19 n = 4 (u) R= NH-CO-$(CH_2)n'$ -CH-$(CH_2)n''$-R'

|
$(CH_2)m$
|
B

wherein

n' = n" = 0

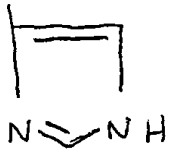
R' = $NH^+_3$

m = 1

B = imidazole

R = NH-CO-CH- $NH_3^+$

|
$CH_2$



(f) R = CO-$CH_3$

u = 11

k = 8

or

i = 19 n = 4 (u) R= NH-CO-(CH$_2$)n' -CH-(CH$_2$)n"-R'

(CH$_2$)m

B

wherein

n' = n" = 0

R' = $NH^+_3$

m = 1

B = imidazole

R = NH-CO-CH- $NH_3^+$

CH$_2$

(f) R = CO-CH$_3$

u = 15

k = 4

or

i = 19 n = 4 (u) R= NH-CO-(CH$_2$)n' -CH-(CH$_2$)n"-R'

(CH$_2$)m

B

wherein

n' = n" = 0

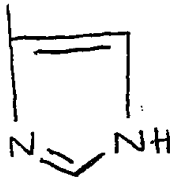
R' = $NH^+_3$

m = 1

B = imidazole

R = NH-CO-CH- $NH_3^+$

CH$_2$



(f) R = CO-(CHOH)rH

r = 5

u = 12

k = 3

or

i = 19 n = 4 (u) R= NH-CO-$(CH_2)$n'-CH-$(CH_2)$n"-R'

$(CH_2)$m

B

wherein

(q) n' = n" = 20

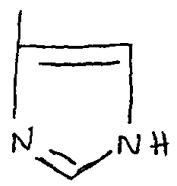
R' = NH-CO-$CH_3$

m = 1

B = imidazole

R = NH-CO-CH- NH-CO-$CH_3$

$CH_2$



(f) R = $NH^+_3$

u = 16

f = 4

k = 3

**9.** Composition containing at least one oligomeric conjugate according to anyone of claims 1 to 8, in association with at least one biological molecule, such as a peptide, an oligoside or an oligonucleotide or a mixture thereof.

**10.** Combined preparation containing as active substance the following individual components, in the form of a kit-of-parts :

- an oligomeric conjugate according to anyone of claims 1 to 8,
- at least one oligomeric conjugate according to anyone of claims 1 to 8, in association with at least one biological molecule, such as a peptide, an oligoside or an oligonucleotide, or a mixture thereof,

for the simultaneous, separate or sequential use, for the *in vitro*, the *in vivo* or the *ex vivo* transfer of said biological molecules into the cytosol and/or cell nucleus.

11. Use of an oligomeric conjugate according to anyone of claims 1 to 8, for the *in vitro*, the *ex vivo* or the *in vivo* intracellular transfer of biological molecules into the cytosol and/or in the cell nucleus.

12. Use of an oligomeric conjugate according to anyone of claims 1 to 8 or of a composition according to claim 9, or of a combined preparation according to claim10, for the intracellular the *in vitro*, the *ex vivo* or the *in vivo* transfer of a peptide, an oligoside or an oligonucleotide, or a mixture thereof, into the cytosol or/and in the cell nucleus.

13. Use of an oligomeric conjugate according to anyone of claims 1 to 8 or of a composition according to claim 9, or of a combined preparation according to claim10, wherein the cells are chosen among muscular, epithelial, endothelial, myeloid cells such as monocytes, macrophages and fibroblasts, leukocytes and granulocytes, osteoblasts as well as dendritic cells, stem cells, neuronal cells, or dermal cells.

14. Method for the *in vivo*, the *in vitro* or the *ex vivo* transfer of an oligonucleotide, wherein an oligonucleotide and an oligomeric conjugate according to anyone of claims 1 to 8 or of a composition according to claim 9, or of a combined preparation according to claim10, are(is) contacted with a medium containing cells to be transferred, under conditions such that there is :

- transfer of an antisense oligonucleotide in the cytosol and/or the cell nucleus where it binds and blocks the complementary mRNA sequence,
- or transfer of an oligonucleotide as activator into the cytosol where it depresses or activates a second messenger in the cytosol, or the corresponding gene in the nucleus,
- or transfer into the cytosol and/or the cell nucleus of oligonucleotides corresponding to a repetitive bacterial type DNA sequence with stimulating or immunodepressive activity,

- or transfer of an oligonucleotide in the cell nucleus where it binds to DNA and forms a triple helix leading to the inhibition of gene expression.

- or transfer into the cytosol and/or the cell nucleus of RNA oligonucleotide acting as decoys which inhibit gene expression by blocking the binding of regulatory factors to the authentic DNA region.

- or transfer into the cytosol and/or the cell nucleus of ribozymes (RNA oligonucleotides) which inhibit gene expression by cleaving the mRNA.

**15.** Method for the *in vivo*, the *in vitro* or the *ex vivo* transfer of peptide, wherein a peptide and an oligomeric conjugate according to anyone of claims 1 to 8 or of a composition according to claim 9, or of a combined preparation according to claim 10, in particular wherein the peptide is an antigenic peptide, are(is) contacted with a medium containing cells to be transferred, under conditions such that there is a transfer of said antigenic peptide in the cytosol of antigen presenting cells (macrophages, dendritic cells and B cells) where they are processed in proteosomes in order to bind to MHCI molecules, allowing the presentation of the antigenic epitope fixed on MHCI.

**16.** Method for the *in vivo*, the *in vitro* or the *ex vivo* transfer of an oligoside, wherein an oligoside and an oligomeric conjugate according to anyone of claims 1 to 8 or of a composition according to claim 9, or of a combined preparation according to claim 10, are(is) contacted with a medium containing cells to be transferred, under conditions such that there is a transfer of said oligoside into the cytosol and/or the cell nucleus.

**17.** Pharmaceutical composition, comprising as active substance at least an oligomeric conjugate according to anyone of claims 1 to 8, or of a composition according to claim 9, or of a combined preparation according to claim10, or in association with a pharmaceutically acceptable vehicle.

18. Use of an oligomeric conjugate according to anyone of claims 1 to 8, or of a composition according to claim 9, or of a combined preparation according to claim10, or for the preparation of a drug for use in the treatment of cancer, inflammatory or immunology diseases (such as graft rejection, allergy, auto-immunity) or infectious diseases.

19. Kit or case containing :

- an oligomeric conjugate according to anyone of claims 1 to 8, substituted by a protonable residue leading in a weak acid medium to a destabilization of cellular membranes, this oligomeric conjugate being able to comprise a recognition signal, which is previously fixed or not on the above-said conjugate, said recognition signal being dependent upon the cell to target,
- at least one biological molecule to transfer,
- optionally reagents enabling the possible binding of the recognition signal on the above-said oligomeric conjugate,
- optionally reagents enabling the formation of a composition according to claim 9, or of a combined preparation according to claim 10,
- reagents enabling the transfer of the biological molecule in the cytosol and/or the cell nucleus.